

REMARKS/ARGUMENTS

Status of the claims

Pursuant to Applicant's election with traverse of Group I, claims 1-17 and 20-21 were previously undergoing examination on the merits. The Examiner withdrew the previously required further election of a species of a TLR receptor 3 and a TLR receptor.

Without acquiescing on the merits, claims 1 to 4, 6 to 9, 11 to 19, and 22 to 24 have been canceled without prejudice. Claims 5, 10, 20, and 21 are currently amended and claims 25 and 26 are new. After entry of these amendments, claims 5, 10, 20, 21, 25 and 26 will be undergoing examination.

Claims 1-17 and 20-21 stand rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-21 stand rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement.

Claims 5-1 7, 20-21 stand rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement.

Claims 1, 3, 4, 13, and 17 stand rejected under 35 U.S.C. 102(a) for allegedly being anticipated by Kawai et al., (Published November 15, 2001, The Journal of Immunology, Volume 167, Issue 10, page 5887-5894)

Claim 20 and 21 stand rejected under 35 U.S.C. 102(a) for allegedly being anticipated by Kawai et al., (Published November 15, 2001, The Journal of Immunology, Volume 167, Issue 10, page 5887-5894).

Claims 1-4, and 13 stand rejected under 35 U.S.C. 102(b) for allegedly being anticipated Navarro et al. (1999, The Journal of Biological Chemistry, Volume 274, Number 50, pages 35535-35538).

Applicants respectfully respond to these grounds of rejection below.

Support for the amendments to the claims

Claims 5 and 20 have been amended to set forth limitations found in their dependent claims. The subject matter of amended claims 10 and 21 finds support in their corresponding previous recitals. New dependent claims 25 and 26 set forth the cell is a macrophage. Support for this subject matter is found *inter alia* in the specification at p. 41 and 42. Accordingly, the Applicants believe the amendments to the claims add no new matter and respectfully request their entry.

Status of the specification

The disclosure stands objected to for containing an embedded hyperlink and/or other form of browser-executable code (see page 7, line 20; page 31, line 29; page 37, line 28). As required, pursuant to MPEP §608.01, the Applicants have filed amendments which delete the embedded hyperlink and/or other form of browser-executable code. Applicants believe these amendments to the specification add no new matter and respectfully request their entry.

Accordingly, the Applicants respectfully request that this grounds of objection be reconsidered and withdrawn.

Objection to claim 1.

Claim 1 stands objected to for reciting "a Toll-like receptors". Claim 1 has been canceled without prejudice. Accordingly, the Applicants respectfully request that this grounds of objection be reconsidered and withdrawn.

Response to the rejection of claims 1-17 and 20-21 under 35 U.S.C. 112, second paragraph, for alleged indefiniteness.

In the spirit of expediting prosecution and without acquiescing on the merits, the pending claims have been amended and now avoid all the recitals at issue in rejections numbered I through XI. Accordingly, the Applicants respectfully request that the above grounds for rejection be reconsidered and withdrawn.

Response to the rejection of claims 20-21 under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement.

In the spirit of expediting prosecution and without acquiescing on the merits, claims 20 and 21 have been amended and now avoid all the recitals at issue. Accordingly, the Applicants respectfully request that the above grounds for rejection be reconsidered and withdrawn.

Response to the rejection of claims 5-17 and 20-21 under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement.

As previously noted by the Action, whether undue experimentation is required to practice an invention is typically determined by evaluating: (i) the relative skill of those in the art; (ii) the nature of the invention; (iii) the breadth of the claims; (iv) the amount of guidance presented; (v) the presence of working examples; (vi) the state of the art; (vii) the predictability of the art; and (viii) the quantity of experimentation necessary. *Ex parte Forman*, 230 U.S.P.Q. 546 (PTO Bd. Pat. App. & Inter. 1986), *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). The Applicants address the Wands factors according to the issues raised by the Action, and thereafter provide the required overall summary assessment of the Wands factors.

Wands factor (i): the relative skill of those in the art.

Applicants believe that the relative skill and experience of those in the applicable medical and technical arts are very high. Such work is typically conducted by research enterprises populated with persons with advanced doctoral and medical training in the relevant fields. Support for this assertion is readily evidenced by the authorship of the art disclosed with the previous IDS and discussed herein.

Wands factor (ii): the nature of the invention.

The invention is in the field of pharmaceuticals. This field of art is traditionally one in which a large volume of testing is both typical and routine. It is a field in which the courts have held that the necessary showing for enablement does not require testing in humans¹.

¹ Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is

Wands factor (iii): the breadth of the claims.

The Action contended that the Applicants' is not enabled because the specification does not provide sufficient guidance for the use of the genus of Toll-like receptors; molecules, and IRF3 cellular responses for the claimed invention." As amended the base claims are drawn to steps of contacting the cell with an imidazoquinoline compound or poly I:C thereby inhibiting a viral infection or replication. These steps are simply performed and do not introduce the concerns identified by the Examiner. With respect to the enablement of the methods as they relate to *bacterial* infections or replication, the claims as amended now set forth *viral* infections.

Wands factor (iv): the amount of guidance presented.

The specification teaches one of ordinary skill in the art all they need to practice the claimed invention. With respect to the remaining Forman factors, the specification provides adequate guidance for all manipulations required to practice the invention by disclosing the therapeutic utilities of the compounds and provides and exemplifies simple *in vitro* tests that are used for screening for the required activity.

Wands factor (v): Working examples.

The specification provides a working example of the inhibition of viral replication in Example 5. Poly (I:C)-treated murine bone marrow-derived macrophages were exposed *in vitro* to murine gammaherpes virus 68. The treatment was found to greatly inhibit viral replication (see, paragraph bridging pages 41 and 42). Additionally, NIH3T3 cells exposed to IFN α / β produced by the treated macrophages also were able to suppress viral replication (see

well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer (In re Brana 34 U.S.P.Q. 2nd 1436 (Fed. Cir. 1995)).

See *Scott v. Finney*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994) ("Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings.").

first full paragraph on p. 42). In this regard, the Applicants note that new dependent claims 25 and 26 set forth that the cell is a macrophage.

Wands factor (vi and vii): State of the art and predictability.

Similar to the Action, the Applicants discuss these two criteria together. Here, the Applicants have shown that their method works. Accordingly, any residual uncertainties in the art as to how the particularly claimed subject matter achieves its effects is largely immaterial.

The MPEP requires more. MPEP §2164.03 at 2100-90, top left column states:

Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable exact correlation is not required, as stated in *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985):

[B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.)

The correlation of the *in vitro* data in the specification and the claimed utility is not spurious but supported by reasoning and in accord with the biology.

MPEP §2164.02 under the heading of Correlation: In vitro/In vivo states:

An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention.

The Applicants submit, with the above MPEP guidance in mind, that one of ordinary skill in the art would appreciate that the specification *does* provide a working example of their invention in the Examples.

Wands factor (viii): quantity of experimentation required

Applicants believe that the amendments to the claims have greatly reduced the amount of experimentation required to practice the invention. The field of the invention is the pharmaceutical arts. A great deal of experimentation is quite routine in this field. It is a field which is largely devoted to the screening and testing of a large number of candidate compounds,

compositions and treatments in model systems². In addition, as noted above, the Courts do not require clinical testing to demonstrate utility.

Overall Summary of the Wands Analysis

Here,

- (i) the relative skill and experience of those in the art of pharmaceuticals is generally quite high;
- (ii) the field of art is traditionally one in which a large volume of compound screening is both typical and routine and a demonstration of clinical efficacy is not required.
- (iii) the breadth of the claims as presently is well commensurate with the disclosure;
- (iv) the disclosure provides adequate guidance for all manipulations required to practice the invention;
- (v) the specification provides working examples as explained above;
- (vi) the state of the art is high enough to practice the invention in view of the Applicant's disclosure;
- (vii) noting that FDA standards as to operability are not those set forth for patentability, the art is sufficiently predictable such that one of ordinary skill in the art would consider the disclosed data to support the operability of the claimed subject matter for the purposes of enablement under 35 U.S.C. § 112, first paragraph;
- (viii) the field of art is one in which a great deal of experimentation is routinely performed by persons of ordinary skill in the art, and the amount of additional effort required to practice the invention is well within the capabilities of those in the field.

Accordingly, Applicants submit that one of ordinary skill in the art can readily practice the invention as claimed using only an amount of experimentation which would be

² Indeed, The Federal Circuit has held that if a specification teaches one embodiment and sets forth a method for determining dose/response, the experimentation required to determine a dose/response curve is not undue, even if the studies proved to cost approximately \$50,000 and took 6-12 months to accomplish. *United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988).

clearly routine in the art. Applicants respectfully request that the above rejection be reconsidered and withdrawn.

Response to the rejection of claims 1, 3, 4, 13, and 17 under 35 U.S.C. 102(a) for allegedly being anticipated by Kawai et al., (Published November 15, 2001, The Journal of Immunology, Volume 167, Issue 10, page 5887-5894).

In the spirit of expediting prosecution and without acquiescing on the merits, claims 1, 3, 4, 13, and 17 have been canceled without prejudice. Accordingly, the Applicants respectfully request that the above grounds for rejection be reconsidered and withdrawn.

Response to the rejection of claims claim 20 and 21 under 35 U.S.C. 102(a) for allegedly being anticipated by Kawai et al., (Published November 15, 2001, The Journal of Immunology, Volume 167, Issue 10, page 5887-5894).

Without acquiescing on the merits and in order to expedite prosecution, claims 20 and 21 have been amended to set forth contacting the cell with an imidazoquinoline compound or poly I:C. This subject matter is not found in the cited reference. Accordingly, the Applicants respectfully request that the above grounds for rejection be reconsidered and withdrawn.

Turning next to the Alexopoulos et al. reference (mentioned in an aside as disclosing poly(I:C) in the context of the TLR3), the Applicants note, with respect to any nonobviousness rejection which might further be alleged over this art, that the reference concludes by stating "The importance of TLR3 in the antiviral response remains to be established. Challenge of TLR-3 deficient mice with a range of viruses would be required to elucidate whether TLR3 has a role in the host's defence against viruses."

Response to the rejection of claims 1-4, and 13 under 35 U.S.C. 102(b) for allegedly being anticipated Navarro et al. (1999, The Journal of Biological Chemistry, Volume 274, Number 50, pages 35535-35538).

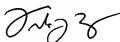
In the spirit of expediting prosecution and without acquiescing on the merits, claims 1, 3, 4, 13, and 17 have been canceled without prejudice. Accordingly, the Applicants respectfully request that the above grounds for rejection be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Frank J. Mycroft
Reg. No. 46,946

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 925-472-5000
Fax: 415-576-0300
Attachments
FJM:kar
61243199 v2